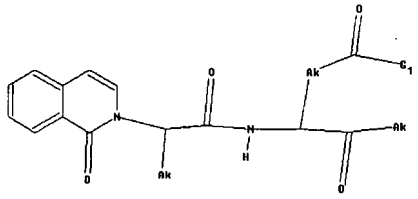
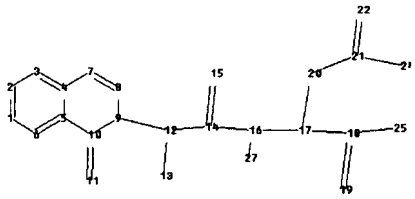
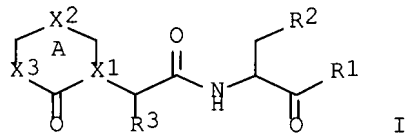
```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *


FILE 'HOME' ENTERED AT 10:40:22 ON 17 OCT 2007

=> file reg
=> Uploading C:\Program Files\Stnexp\Queries\Queries\10743563.str
```



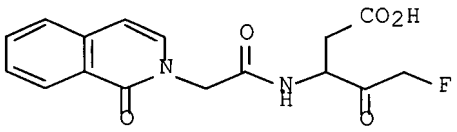


```
chain nodes :
11  12  13  14  15  16  17  18  19  20  21  22  24  25  27
ring nodes :
1  2  3  4  5  6  7  8  9  10
chain bonds :
9-12  10-11  12-13  12-14  14-15  14-16  16-17  16-27  17-18  17-20  18-19  18-25
20-21  21-22  21-24
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10
exact/norm bonds :
4-7  5-10  7-8  8-9  9-10  9-12  10-11  12-13  14-15  14-16  16-17  17-20  18-19
18-25  20-21  21-22  21-24
exact bonds :
12-14  16-27  17-18
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6
isolated ring systems :
containing 1 :


G1:O,N

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS  22:CLASS  24:CLASS  25:CLASS  27:CLASS




L1      STRUCTURE UPLOADED

=> s l1 sam
L2            4 SEA SSS SAM L1

=> s l1 full
L3           51 SEA SSS FUL L1
```

```
=> file caplus

=> s l3
L4            8 L3

=> s l4 and pd<dec 2002
      22839189 PD<DEC 2002
                  (PD<20021200)
L5            1 L4 AND PD<DEC 2002

=> dis l5 bib abs hitstr

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2001:435047  CAPLUS  Full-text
DN   135:46192
TI   Synthesis and use of heterocyclic substituted-amido halopentanoate
     derivatives as caspase inhibitors
IN   Golec, Julian; Charifson, Paul; Charrier, Jean-Damien; Binch, Hayley
PA   Vertex Pharmaceuticals Incorporated, USA
SO   PCT Int. Appl., 88 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2001042216        A2    20010614    WO 2000-US33260        20001208 <--
     WO 2001042216        A3    20020228
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2393710           A1    20010614    CA 2000-2393710        20001208 <--
     BR 2000016282        A     20020827    BR 2000-16282          20001208 <--
     EP 1244626           A2    20021002    EP 2000-988026         20001208 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003516393        T     20030513    JP 2001-543517         20001208
     HU 2003000782        A2    20030929    HU 2003-782            20001208
     HU 2003000782        A3    20031128
     NZ 519424            A     20040326    NZ 2000-519424         20001208
     NZ 530485            A     20060224    NZ 2000-530485         20001208
     ZA 2002004390        A     20030602    ZA 2002-4390           20020531
     NO 2002002656        A     20020806    NO 2002-2656           20020605 <--
     IN 2002KN00759       A     20050311    IN 2002-KN759          20020605
     MX 2002PA05779       A     20050908    MX 2002-PA5779         20020610
     AU 2006225317        A1    20061102    AU 2006-225317         20061010
PRAI US 1999-169812P      P     19991208
     AU 2001-24283        A3    20001208
     NZ 2000-519424       A1    20001208
     WO 2000-US33260      W     20001208
OS   MARPAT 135:46192
GI
```



I



II

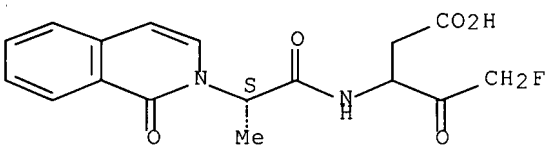
AB Compds. I and their synthesis are claimed [wherein; R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, COOH (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. For instance; substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1,-3,-7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μM for IL-1β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

IT 344461-03-6P 344461-10-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and use of heterocyclic substituted-amido halopentanoate derivs. as caspase inhibitors)

RN 344461-03-6 CAPLUS

CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

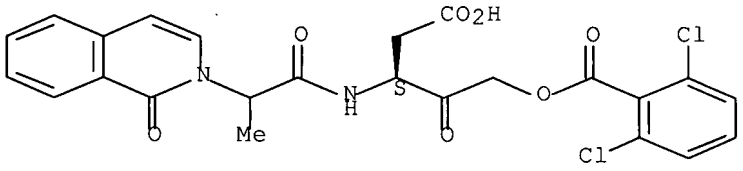
Absolute stereochemistry.



RN 344461-10-5 CAPLUS

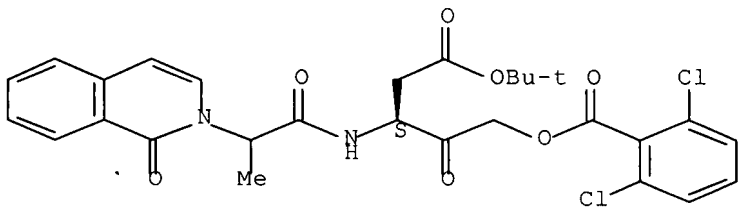
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-2-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]butyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 344461-30-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and use of heterocyclic substituted-amido halopentanoate derivs. as caspase inhibitors)
RN 344461-30-9 CAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-5-(1,1-dimethylethoxy)-2,5-dioxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]pentyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> s l4 not l5
L6 7 L4 NOT L5

=> dis l6 1-7 bib abs fhitstr

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:593290 CAPLUS Full-text
DN 147:202903
TI Exploring Peptide-likeness of Active Molecules Using 2D Fingerprint Methods
AU Eckert, Hanna; Bajorath, Juergen
CS Department of Life Science Informatics, Rheinische Friedrich-Wilhelms-Universitaet, Bonn, D-53113, Germany
SO Journal of Chemical Information and Modeling (2007), 47(4), 1366-1378
CODEN: JCISD8; ISSN: 1549-9596
PB American Chemical Society
DT Journal
LA English
AB Similarity searching for peptide-like small mols. is a difficult task because the amide backbone shared by these mols. tends to mask features that determine biol. activity. The authors have investigated 2D fingerprints for their ability to differentiate between peptide-like mols. having different activity or to facilitate a peptidomimetic transition from mols. with strong peptide character to compds. having little or none. For these purposes, different

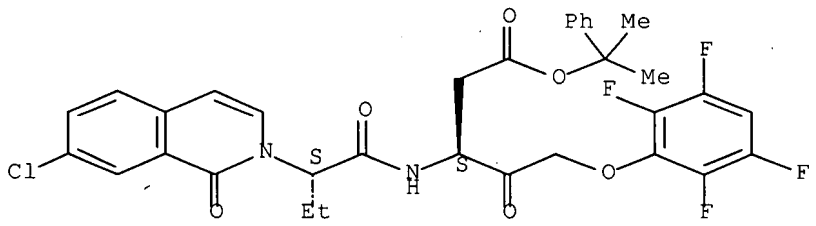
compound activity classes were assembled consisting of mols. having strong, moderate, and weak peptide character. For the quantification of peptide character, a "peptide flavor" index was introduced. In systematic search calcns., an encouraging finding has been that most of the investigated 2D fingerprints were capable of distinguishing between peptide-like mols. having different activities. However, only two fingerprints of different design also displayed a strong tendency to detect mols. with decreasing peptide character. One of these search tools is a recently introduced property descriptor-based fingerprint that showed two addnl. advantages: its flexible design could be adjusted to increasingly recover mols. with little peptide-likeness, and in addition, its search performance was not affected by differences in mol. size.

IT 721398-07-8
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(exploring peptide-likeness of active mols. using 2D fingerprint methods)

RN 721398-07-8 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)-, 1-methyl-1-phenylethyl ester, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:150976 CAPLUS Full-text
DN 146:235880
TI Preparation of caspase inhibitor prodrugs
IN Durrant, Steven; Charrier, Jean-Damien; Studley, John
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 49pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007015931	A2	20070208	WO 2006-US28174	20060720
WO 2007015931	A3	20070607		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 2007155718 A1 20070705 US 2006-489939 20060720

PRAI US 2005-703375P P 20050728

OS MARPAT 146:235880

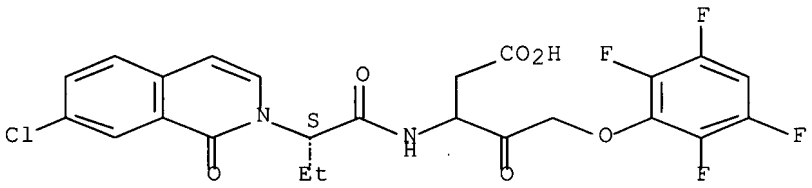
AB This invention relates to prodrugs of caspase inhibitors comprising of a furo [3,2-d]oxazolin-5-one moiety which, under specific conditions, can convert into biol. active compds., particularly caspase inhibitors. This invention also relates to the processes for preparing these prodrugs of caspase inhibitors. This invention further relates to pharmaceutical compns. comprising said prodrugs and to the use thereof for the treatment of diseases related to inflammatory or degenerative conditions. Trifluoroacetic anhydride was added to a solution of (S)-carbazole-9- carboxylicacid 1-(1-carboxymethyl-3-fluoro-2-oxo-propylcarbamoyl)-2-methyl- Pr ester in anhydrous dichloromethane under a nitrogen atmosphereat ambient temperature After one hour, the reaction was diluted with anhydrous dichloromethane and tris-(2-aminoethyl)amine polystyrene resin was added and the reaction was stirred for a furtherone hour. The resin was removed by filtration and thefiltrate concentrated in vacuo and triturated with dichloromethane and petroleum ether to give (S)-carbazole-9-carboxylic acid 1-(3a-fluoromethyl-5-oxo-3a,5,6,6a-tetrahydro-furo[3,2-d]oxazol-2-yl)-2- methyl-propylester as a white solid.

IT 618460-08-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of caspase inhibitor prodrugs)

RN 618460-08-5 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)- (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:565214 CAPLUS Full-text

DN 141:106388

TI Preparation of 4-oxo-3-(1-oxo-1H-isoquinolin-2-ylacetylamino)-pentanoic acid ester and amide derivatives as caspase inhibitors

IN Charrier, Jean-Damien; Mortimore, Michael; Studley, John R.

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004058718	A1	20040715	WO 2003-US40870	20031222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

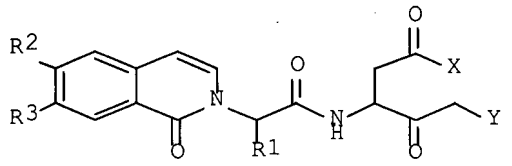
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

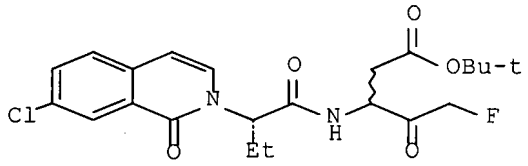
CA 2511235	A1	20040715	CA 2003-2511235	20031222
AU 2003303345	A1	20040722	AU 2003-303345	20031222
US 2004192612	A1	20040930	US 2003-743563	20031222
EP 1581501	A1	20051005	EP 2003-814289	20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1745065	A	20060308	CN 2003-80109285	20031222
JP 2006513220	T	20060420	JP 2004-563916	20031222
JP 2007070368	A	20070322	JP 2006-343613	20061220
PRAI US 2002-435133P	P	20021220		
JP 2004-563916	A3	20031222		
WO 2003-US40870	W	20031222		

OS MARPAT 141:106388

GI



I



II

AB The title compds. of formula I [X = alkoxy, (substituted) NH2, etc.; Y = halo, trifluorophenoxy, tetrafluorophenoxy; R1 = alkyl; R2, R3 = H, halo, OCF3, CN, CF3] are prepared The present invention also provides pharmaceutical compns. and methods using such compns. for treating a caspase-mediated disease, particularly in the central nervous system. Thus, II was prepared from 7-chloroisochromen-1-one (preparation given), (S)-2-aminobutyric acid tert-Bu ester and 3-amino-5-fluoro-4- hydroxypentanoic acid tert-Bu ester.

IT 640286-59-5P

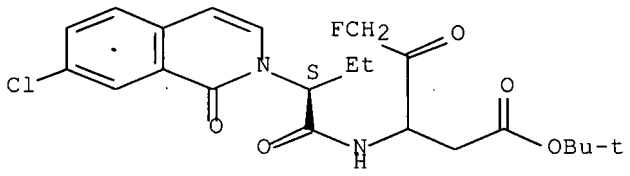
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of (oxoisoquinolinylacetylamino)-oxopentanoic acid ester and amide derivs. as caspase inhibitors)

RN 640286-59-5 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo-, 1,1-dimethylethyl ester (CA INDEX NAME)

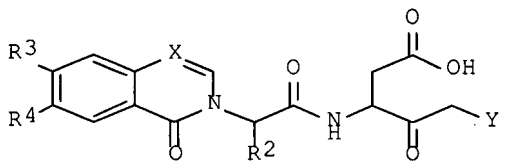
Absolute stereochemistry.



L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:20662 CAPLUS Full-text
DN 140:77410
TI Preparation of isoquinolinone and quinazolinone peptide derivatives as caspase inhibitors
IN Knegtel, Ronald; Mortimore, Michael; Studley, John; Millan, David
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002961	A1	20040108	WO 2003-US20557	20030627
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2493646	A1	20040108	CA 2003-2493646	20030627
	AU 2003248758	A1	20040119	AU 2003-248758	20030627
	US 2004072850	A1	20040415	US 2003-609147	20030627
	BR 2003012232	A	20050510	BR 2003-12232	20030627
	EP 1539701	A1	20050615	EP 2003-762231	20030627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1675184	A	20050928	CN 2003-818793	20030627
	JP 2005533825	T	20051110	JP 2004-518103	20030627
	NZ 537807	A	20070531	NZ 2003-537807	20030627
	MX 2005PA00069	A	20050411	MX 2005-PA69	20050103
	IN 2005KN00083	A	20050916	IN 2005-KN83	20050124
	NO 2005000851	A	20050329	NO 2005-851	20050217
PRAI	US 2002-392592P	P	20020628		
	US 2002-435073P	P	20021220		
	WO 2003-US20557	W	20030627		

OS MARPAT 140:77410
GI



I

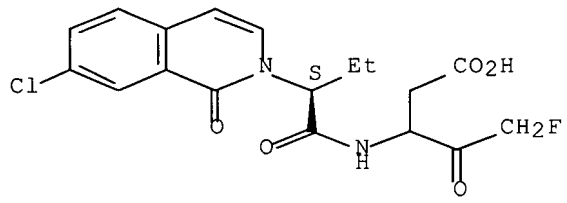
AB The invention relates to isoquinolinones and quinazolinones I [X is CH or N; Y is halo, tri- or tetrafluorophenoxy; R2 is alkyl; R3 is H, halo, OCF3, CN, or CF3; R4 is groups R3 or alkylthio, (un)substituted Ph, phenoxy, or phenylthio; with the proviso that when Y is halo, then R3 and R4 are not both H] which are caspase inhibitors useful in compns. for the treatment of various diseases, conditions, or disorders. Thus, I (X = CH, Y = F, R2 = Et, R3 = H, R4 = Cl), prepared by coupling of (S)-2-(7-chloro-1-oxo-1H-isoquinolin-2-yl)butyric acid (preparation given) with 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester, had Ki (M-1 s-1) > 500,000 for inhibition of caspase-1 or caspase-3, Ki 100,000-500,000 for inhibition of caspase-8, and IC50 < 1 μM for inhibition of interleukin-1β secretion.

IT 618459-84-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoquinolinone and quinazolinone peptide derivs. as caspase inhibitors)

RN 618459-84-0 CAPLUS

CN Pentanoic acid, 3-[[(2S)-2-(7-chloro-1-oxo-2(1H)-isoquinolinyl)-1-oxobutyl]amino]-5-fluoro-4-oxo- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:991174 CAPLUS Full-text

DN 140:28050

TI Synthesis of peptide heterocyclic derivatives as caspase inhibitors

IN Golec, Julian M. C.; Charifson, Paul S.; Charrier, Jean-Damien; Binch, Hayley

PA UK

SO U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO

DT Patent

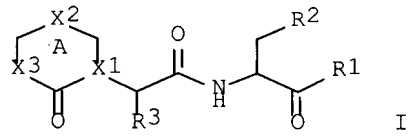
LA English

FAN.CNT 1

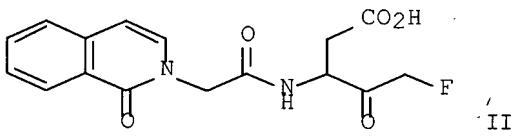
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003232846	A1	20031218	US 2002-166437	20020610
PRAI	US 2002-166437		20020610		

OS MARPAT 140:28050

GI



I



II

AB Compds. I and their synthesis are claimed [R1 = H, CN, CHN2, (substituted)alkyl, aryl, non-aromatic heterocycle, etc.; R2 = CH2COOH, CO2H (or ester/amide/isosteres of); R3 = H or alkyl; X1, X3 = N or C; X2 = bond, O, S, N or C wherein any X with suitable valence may bear a substituent; each C in ring A may also be substituted; ring A substituents = H, halo, alkyl, aryl, OH, CN, etc.; A may also bear a fused ring]. Over 20 synthetic examples are given. Thus, substitution of bromoacetic acid Et ester with the corresponding isoquinolone followed by saponification and coupling to 3-amino-5-fluoro-4-hydroxypentanoic acid tert-Bu ester provided the hydroxy ester intermediate. Oxidation of the hydroxy ester followed by treatment with TFA yielded II as a white powder. Compds. of the invention are caspase inhibitors; data is provided for caspase-1,-3,-7 and caspase-8 inhibition (Ki). Also determined was inhibition of IL-1β secretion from peripheral blood mononuclear cells and activity in a Fas ligand induced apoptosis assay. Compound II had Ki (M-1 s-1) of 248,000 for caspase-1, 130,000 for caspase-3 and an IC50 of 2.9 μM for IL-1β secretion. Compds. I may be used as a component of immunotherapy for the treatment of cancer.

IT 344461-03-6P

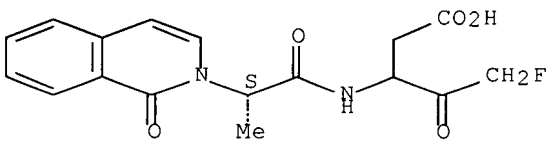
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of peptide heterocyclic derivs. as caspase inhibitors)

RN 344461-03-6 CAPLUS

CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

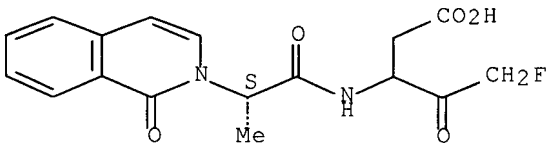


L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:855766 CAPLUS Full-text
DN 139:345913
TI Identification of tumor necrosis factor α (TNF-α) modulator compounds, and use for treatment of TNF-mediated diseases
IN Miller, Karen; Diu-Hercend, Anita; Hercend, Thierry; Lang, Paul; Weber, Peter; Golec, Julian; Mortimore, Michael
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 268 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003088917	A2	20031030	WO 2003-US12262	20030417
	WO 2003088917	A3	20040304		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003225088	A1	20031103	AU 2003-225088	20030417
	US 2004048797	A1	20040311	US 2003-419327	20030417
	EP 1499898	A2	20050126	EP 2003-721795	20030417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-374434P	P	20020419		
	WO 2003-US12262	W	20030417		

AB The invention discloses methods for identifying compds. useful for regulating TNF-α levels and/or activity. The invention also discloses methods for decreasing TNF-α levels and/or activity. Compds. and compns. of the invention are useful for treating TNF-mediated diseases. The invention further discloses kits comprising the compds. and compns. herein and a tool for measuring TNF-α activity and/or levels. Preparation of selected compds., e.g. [3S/R,(2S)]-5-fluoro-4-oxo-3-[(1- (phenothiazine-10-carbonyl)piperidine-2-carbonyl)amino]pentanoic acid, is described.
IT 344461-03-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TNF-α modulator compound identification methods, and use for treatment of TNF-mediated diseases)
RN 344461-03-6 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[(2S)-1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

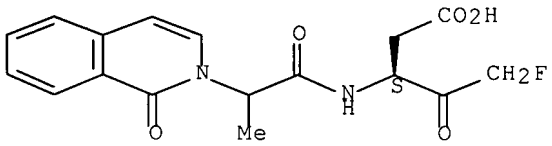


L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:656594 CAPLUS Full-text
DN 139:191460
TI Phospholipids as caspase inhibitor prodrugs
IN Mortimore, Michael; Golec, Julian M. C.
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 256 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003068242	A1	20030821	WO 2003-US4457	20030211
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003211052	A1	20030904	AU 2003-211052	20030211
	US 2004019017	A1	20040129	US 2003-366192	20030211
	EP 1485107	A1	20041215	EP 2003-739810	20030211
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-355889P	P	20020211		
	WO 2003-US4457	W	20030211		

OS MARPAT 139:191460
AB The invention relates to compds. which are prodrugs of caspase inhibitors and pharmaceutically acceptable salts thereof. The invention further relates to the release of caspase inhibitors from these compds. through selective bond cleavage. The invention further relates to pharmaceutical compns. comprising these compds., which are particularly well-suited for treatment of caspase-mediated diseases, including inflammatory and degenerative diseases. The invention further relates to methods for preparing compds. of this invention.
IT 582317-55-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phospholipids as caspase inhibitor prodrugs)
RN 582317-55-3 CAPLUS
CN Pentanoic acid, 5-fluoro-4-oxo-3-[[1-oxo-2-(1-oxo-2(1H)-isoquinolinyl)propyl]amino]-, (3S)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y
STN INTERNATIONAL LOGOFF AT 10:42:20 ON 17 OCT 2007